# **Claims**

1. A bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof:

$$A = \begin{cases} A & \text{(1)} \\ A & \text{(2)} \end{cases}$$

5 wherein

10

15

20

A represents

$$Q_3 \longrightarrow Q_4 \longrightarrow Q_5 \longrightarrow Q_5$$

wherein

Q<sub>1</sub> and Q<sub>4</sub> independently represent direct bond or methylene;

Q<sub>2</sub> represents CHR<sup>2</sup>, or CO,

Q<sub>3</sub> represents CHR<sup>3</sup>, or CO,

wherein

R<sup>2</sup> represents hydrogen, hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkanoyloxy, or C<sub>1-6</sub> alkyl optionally substituted by hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkanoyloxy or mono-, di-, or tri- halogen;

R<sup>3</sup> represents hydrogen, hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkanoyloxy, or C<sub>1-6</sub> alkyl optionally substituted by hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkanoyloxy or mono-, di-, or tri- halogen;

with the proviso that

Q<sub>1</sub> and Q<sub>4</sub> can not be direct bond at the same time;

R<sup>2</sup> and R<sup>3</sup> can not be hydrogen at the same time;

when Q<sub>1</sub> represents direct bond,

10

R³ represents hydroxy, C<sub>1-6</sub> alkoxy or C<sub>1-6</sub> alkanoyloxy;

Q<sub>5</sub> represents CH or CR<sup>5</sup>,

wherein

R5 represents hydroxy, C1-6 alkoxy, C1-6 alkanoyloxy,

or  $C_{1-6}$  alkyl optionally substituted by hydroxy,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyloxy or mono-, di-, or tri-halogen;

Q<sub>6</sub> represents CH or CR<sup>6</sup>,

wherein

R<sup>6</sup> represents hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkanoyloxy,

or  $C_{1-6}$  alkyl optionally substituted by hydroxy,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyloxy or mono-, di-, or tri- halogen;

with the proviso that Q5 and Q6 can not be CH at the same time;

m represents an integer from 0 to 3;

p represents an integer 0 or 1;

15 -X- represents a bond, -O- or -N( $\mathbb{R}^4$ )-,

wherein

R<sup>4</sup> represents hydrogen or C<sub>1-6</sub> alkyl,

with the proviso that when m is 0, -X- represents a bond; and

-Y- represents CH<sub>2</sub>, O or NH; and

20 R<sup>1</sup> represents aryl or heteroaryl,

wherein

said aryl and heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halogen, nitro, hydroxy, carboxy, cyano, amino, N-(C<sub>1-6</sub>alkyl)amino, N,N-

10

15

di( $C_{1-6}$ alkyl)amino, N-( $C_{3-8}$  cycloalkyl)amino,  $C_{1-6}$ alkoxycarbonyl, sulfonamide,  $C_{1-6}$  alkanoyl, N-( $C_{1-6}$ alkanoyl)amino, carbamoyl,  $C_{1-6}$  alkylcarbamoyl,  $C_{3-8}$ cycloalkyl, heterocycle,

C<sub>1-6</sub> alkyl [wherein said alkyl is optionally substituted by cyano, nitro, hydroxy, carboxy, amino, C<sub>1-6</sub> alkoxycarbonyl or mono-, di-, or tri-halogen],

C<sub>1-6</sub> alkoxy [wherein said alkoxy is optionally substituted by mono-, di-, or tri- halogen],

C<sub>1-6</sub> alkylthio [wherein said alkylthio is optionally substituted by mono-, di-, or tri- halogen],

phenyl, benzyl and phenoxy,

[wherein said phenyl, phenyl moiety of said benzyl or phenyl moiety of said phenoxy are optionally substituted by halogen, nitro, hydroxy, carboxy, amino, N-(C<sub>1-6</sub>alkyl)amino, N,N-di(C<sub>1-6</sub> alkyl)amino, N-(C<sub>3-8</sub>cycloalkyl)amino, C<sub>1-6</sub> alkoxycarbonyl, C<sub>1-6</sub>alkoxycarbonyl or C<sub>1-6</sub> alkyl].

2. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

wherein

20 A represents

$$Q_2$$
 $Q_1$ 
or  $Q_5$ 

Q<sub>1</sub> and Q<sub>4</sub> represent methylene;

Q<sub>2</sub> represents CHR<sup>2</sup> or CO,

wherein

PCT/EP2004/012050

- 49 -

				represents hydrogen, hydroxy, $C_{1-6}$ alkoxy, $C_{1-6}$ alkanoyloxy or $C_{1-6}$ alkyl optionally substituted by mono-, di-, or tri- halogen;	
		Q <sub>3</sub>	represents CHR <sup>3</sup> or CO,		
5			wherein		
				represents hydroxy, $C_{1-6}$ alkoxy, $C_{1-6}$ alkanoyloxy, or $C_{1-6}$ alkyl optionally substituted by mono-, di-, or tri- halogen;	
		Q <sub>5</sub>	represen	ts CH;	
	٠	Q <sub>6</sub>	represen	ts CR <sup>6</sup> ,	
10	wherein				
			R <sup>6</sup>	represents hydroxy, $C_{1-6}$ alkoxy, $C_{1-6}$ alkanoyloxy, or $C_{1-6}$ alkyl optionally substituted by mono-, di-, or tri- halogen;	
	m	r	epresents an int	teger from 0 to 3;	
	p	r	epresents an int	teger 0 or 1;	
15	-X-	represents a bond, -O- or -N(R <sup>4</sup> )-,			
		w	wherein		
		R	$R^4$ represents hydrogen or $C_{1-6}$ alkyl, with the proviso that when m is 0, -X- represents a bond;		
		w			
	-Y-	re	presents CH <sub>2</sub> , C	O or NH; and	
20	$R^1$	r	epresents pheny	yl, naphthyl, pyridyl, or pyrimidyl,	
		v	vherein	·	
25			ne or more sub of halogen, ni	ohthyl, pyridyl or pyrimidyl are optionally substituted with estituents independently selected from the group consisting tro, hydroxy, carboxy, cyano, amino, N- $(C_{1-6}$ alkyl)amino, l)amino, N- $(C_{3-8}$ cycloalkyl)amino, $C_{1-6}$ alkoxycarbonyl,	

sulfonamide,  $C_{1-6}$  alkanoyl, N-( $C_{1-6}$ alkanoyl)amino, carbamoyl,  $C_{1-6}$  alkyl-carbamoyl,  $C_{3-8}$ cycloalkyl, heterocycle,

C<sub>1-6</sub> alkyl [wherein said alkyl is optionally substituted by cyano, nitro, hydroxy, carboxy, amino, C<sub>1-6</sub> alkoxycarbonyl or mono-, di-, or tri-halogen],

C<sub>1-6</sub> alkoxy [wherein said alkoxy is optionally substituted by mono-, di-, or tri-halogen],

C<sub>1-6</sub> alkylthio [wherein said alkylthio is optionally substituted by mono-, di-, or tri- halogen],

phenyl, benzyl and phenoxy,

[wherein said phenyl, phenyl moiety of said benzyl or phenyl moiety of said phenoxy are optionally substituted by halogen, nitro, hydroxy, carboxy, amino,  $N-(C_{1-6}alkyl)$ amino,  $N,N-di(C_{1-6}alkyl)$ amino,  $N-(C_{3-8}$  cycloalkyl)amino,  $C_{1-6}$  alkoxycarbonyl,  $C_{1-6}$  alkoxycarbonyl or  $C_{1-6}$  alkyl].

3. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

wherein

A represents

$$Q_3$$
 $Q_2$ 
 $Q_1$ 

Q<sub>1</sub> represents methylene;

Q<sub>4</sub> represents direct bond;

Q<sub>2</sub> represents CHR<sup>2</sup> or CO,

wherein

R<sup>2</sup> represents hydroxy, C<sub>1-6</sub> alkoxy or C<sub>1-6</sub> alkanoyloxy;

10

5

15

20

25

Q<sub>3</sub> represents CHR<sup>3</sup>,

wherein

R<sup>3</sup> represents hydrogen;

- m represents an integer from 0 to 3;
- 5 p represents an integer 0 or 1;
  - -X- represents a bond, -O- or -N(R<sup>4</sup>)-,

wherein

R<sup>4</sup> represents hydrogen or C<sub>1-6</sub> alkyl,

with the proviso that when m is 0, -X- represents a bond;

- 10 -Y- represents CH<sub>2</sub>, O or NH; and
  - R<sup>1</sup> represents phenyl, naphthyl, pyridyl, or pyrimidyl,

### wherein

said phenyl, naphthyl, pyridyl or pyrimidyl are optionally substituted with one or more substituents independently selected from the group consisting of halogen, nitro, hydroxy, carboxy, cyano, amino, N- $(C_{1-6}$ alkyl)amino, N,N-di $(C_{1-6}$ alkyl)amino, N- $(C_{3-8}$  cycloalkyl)amino,  $C_{1-6}$ alkoxycarbonyl, sulfonamide,  $C_{1-6}$  alkanoyl, N- $(C_{1-6}$ alkanoyl)amino, carbamoyl,  $C_{1-6}$ alkylcarbamoyl,  $C_{3-8}$ cycloalkyl, heterocycle,

C<sub>1-6</sub> alkyl [wherein said alkyl is optionally substituted by cyano, nitro, hydroxy, carboxy, amino, C<sub>1-6</sub> alkoxycarbonyl or mono-, di-, or tri-halogen],

C<sub>1-6</sub> alkoxy [wherein said alkoxy is optionally substituted by mono-, di-, or tri- halogen],

C<sub>1-6</sub> alkylthio [wherein said alkylthio is optionally substituted by mono-, di-, or tri- halogen],

phenyl, benzyl and phenoxy,

20

15

25

[wherein said phenyl, phenyl moiety of said benzyl or phenyl moiety of said phenoxy are optionally substituted by halogen, nitro, hydroxy, carboxy, amino, N-(C<sub>1-6</sub>alkyl)amino, N,N-di(C<sub>1-6</sub> alkyl)amino, N-(C<sub>3-8</sub> cycloalkyl)amino, C<sub>1-6</sub> alkoxycarbonyl, C<sub>1-6</sub> alkoxycarbonyl or C<sub>1-6</sub> alkyl].

5

4. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

wherein

A represents

$$Q_3 \xrightarrow{Q_4} Q_1$$

10

Q<sub>1</sub> and Q<sub>4</sub> represents methylene;

Q<sub>2</sub> represents CHR<sup>2</sup>,

wherein

R<sup>2</sup> represents hydrogen;

15

Q<sub>3</sub> represents CHR<sup>3</sup>,

wherein

- $R^3$  represents hydrogen, hydroxy,  $C_{1-6}$  alkoxy or  $C_{1-6}$  alkanoyloxy;
- m represents an integer from 0 to 3;
- p represents an integer 0 or 1;
- 20 -X- represents a bond, -O- or -N( $\mathbb{R}^4$ )-,

wherein R<sup>4</sup> is hydrogen or C<sub>1-6</sub> alkyl,

with the proviso that when m is 0, -X- represents a bond;

-Y- represents CH<sub>2</sub>, O or NH; and

10

15

20

R<sup>1</sup> represents phenyl, naphthyl, pyridyl, or pyrimidyl,

#### wherein

said phenyl, naphthyl, pyridyl or pyrimidyl are optionally substituted with one or more substituents independently selected from the group consisting of halogen, nitro, hydroxy, carboxy, cyano, amino, N-( $C_{1-6}$ alkyl)amino, N,N-di( $C_{1-6}$ alkyl)amino, N-( $C_{3-8}$  cycloalkyl)amino,  $C_{1-6}$ alkoxycarbonyl, sulfonamide,  $C_{1-6}$  alkanoyl, N-( $C_{1-6}$ alkanoyl)amino, carbamoyl,  $C_{1-6}$ alkylcarbamoyl,  $C_{3-8}$ cycloalkyl, heterocycle,

C<sub>1-6</sub> alkyl [wherein said alkyl is optionally substituted by cyano, nitro, hydroxy, carboxy, amino, C<sub>1-6</sub> alkoxycarbonyl or mono-, di-, or tri-halogen],

C<sub>1-6</sub> alkoxy [wherein said alkoxy is optionally substituted by mono-, di-, or tri- halogen],

C<sub>1-6</sub> alkylthio [wherein said alkylthio is optionally substituted by mono-, di-, or tri- halogen],

phenyl, benzyl and phenoxy,

[wherein said phenyl, phenyl moiety of said benzyl or phenyl moiety of said phenoxy are optionally substituted by halogen, nitro, hydroxy, carboxy, amino, N- $(C_{1-6}$ alkyl)amino, N,N-di $(C_{1-6}$  alkyl)amino, N- $(C_{3-8}$  cycloalkyl)amino, C<sub>1-6</sub> alkoxy-carbonyl, C<sub>1-6</sub> alkoxycarbonyl or C<sub>1-6</sub> alkyl].

5. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

## wherein

### 25 A represents

$$Q_3$$
 $Q_2$ 
 $Q_1$ 

20

Q<sub>1</sub> and Q<sub>4</sub> represent methylene;

Q<sub>2</sub> represents CHR<sup>2</sup>,

wherein

R<sup>2</sup> represents hydroxy, C<sub>1-6</sub> alkoxy or C<sub>1-6</sub> alkanoyloxy;

Q<sub>3</sub> represents CHR<sup>3</sup>,

wherein

R<sup>3</sup> represents hydrogen;

m represents an integer from 1 to 3;

p represents 0 or 1;

-X- represents a bond, -O- or -N(R<sup>4</sup>)-,

wherein

R4 is hydrogen or C1-6 alkyl,

with the proviso that when m is 0, -X- represents a bond;

15 -Y- represents CH<sub>2</sub>, O or NH; and

R<sup>1</sup> represents phenyl, naphthyl, pyridyl, or pyrimidyl,

wherein

said phenyl, naphthyl, pyridyl or pyrimidyl are optionally substituted with one or more substituents independently selected from the group consisting of halogen, nitro, hydroxy, carboxy, cyano, amino, N- $(C_{1-6}$ alkyl)amino, N,N-di $(C_{1-6}$ alkyl)amino, N- $(C_{3-8}$  cycloalkyl)amino,  $C_{1-6}$ alkoxycarbonyl, sulfonamide,  $C_{1-6}$  alkanoyl, N- $(C_{1-6}$ alkanoyl)amino, carbamoyl,  $C_{1-6}$ alkylcarbamoyl,  $C_{3-8}$ cycloalkyl, heterocycle,

10

20

C<sub>1-6</sub> alkyl [wherein said alkyl is optionally substituted by cyano, nitro, hydroxy, carboxy, amino, C<sub>1-6</sub> alkoxycarbonyl or mono-, di-, or tri-halogen],

C<sub>1-6</sub> alkoxy [wherein said alkoxy is optionally substituted by mono-, di-, or tri- halogen],

C<sub>1-6</sub> alkylthio [wherein said alkylthio is optionally substituted by mono, di-, or tri- halogen],

phenyl, benzyl and phenoxy,

[wherein said phenyl, phenyl moiety of said benzyl or phenyl moiety of said phenoxy are optionally substituted by halogen, nitro, hydroxy, carboxy, amino, N- $(C_{1-6}$ alkyl)amino, N,N-di $(C_{1-6}$ alkyl)amino, N- $(C_{3-8}$ cycloalkyl)amino, C<sub>1-6</sub>alkoxy-carbonyl, C<sub>1-6</sub> alkoxycarbonyl or C<sub>1-6</sub> alkyl].

6. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

wherein

A represents

Q<sub>5</sub> represents CH;

Q<sub>6</sub> represent CR<sup>6</sup>,

wherein

 $R^6$  represents hydroxy,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyloxy, or  $C_{1-6}$  alkyl optionally substituted by hydroxy,  $C_{1-6}$  alkoxy or  $C_{1-6}$  alkanoyloxy;

- m represents an integer from 0 to 3;
- p represents an integer 0 or 1;

-X- represents a bond, -O- or -N(R<sup>4</sup>)-,

wherein

R<sup>4</sup> represents hydrogen or C<sub>1-6</sub> alkyl,

with the proviso that when m is 0, -X- represents a bond;

-Y- represents NH, O or CH<sub>2</sub>; and

R<sup>1</sup> represents phenyl, naphthyl, pyridyl, or pyrimidyl,

wherein

said phenyl, naphthyl, pyridyl, or pyrimidyl are optionally substituted by one or two of substituents selected from the group consisting of halogen, nitro,  $C_{1-6}$ alkyl, trifluoro $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, trifluoro $C_{1-6}$ alkoxy and  $C_{1-6}$ alkanoylamino.

7. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

wherein

A represents

$$Q_3$$
 $Q_4$ 
 $Q_2$ 
 $Q_1$ 
or  $Q_5$ 

15

5

10

Q<sub>1</sub> and Q<sub>4</sub> represents methylene;

Q<sub>2</sub> represents CHR<sup>2</sup>,

wherein

R<sup>2</sup> represents hydrogen;

20

Q<sub>3</sub> represents CHR<sup>3</sup>,

wherein

R<sup>3</sup> represents hydrogen, hydroxy, C<sub>1-6</sub> alkoxy or C<sub>1-6</sub> alkanoyloxy;

Q<sub>5</sub> represents CH;

Q<sub>6</sub> represents CR<sup>6</sup>,

wherein

R<sup>6</sup> represents hydroxy;

- 5 m represents an integer 2;
  - p represents an integer 0;
  - -X- represents a bond, -O- or -N(R<sup>4</sup>)-,

wherein

R<sup>4</sup> is hydrogen or C<sub>1-6</sub> alkyl,

with the proviso that when m is 0, -X- represents a bond;

- -Y- represents NH or O; and
- R<sup>1</sup> represents phenyl, naphthyl, pyridyl, or pyrimidyl,

wherein

15

20

said phenyl, naphthyl, pyridyl, or pyrimidyl are optionally substituted by one or two of substituents selected from the group consisting of chloro, bromo, fluoro, nitro, methyl, methoxy, trifluoromethyl, trifluoroethyl, trifluoromethoxy, trifluoroethoxy, acetamido and propionylamino;

8. The bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1, wherein said bicyclic amide, carbamate or urea derivative of the formula (I) is selected from the group consisting of:

N-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-N'-[4-(trifluoromethyl)benzyl]urea;

4-(trifluoromethyl)benzyl(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)carbamate:

N-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-[4-(trifluoromethyl)phenyl]propanamide;

N-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-N'-(2-{[4-(trifluoromethyl)phenyl]-amino}ethyl)urea;

N-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-N'-{2-[4-(trifluoromethyl)phenoxy]-ethyl}urea;

- 5 2-{[4-(trifluoromethyl)phenyl]amino}ethyl(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)carbamate;
  - 2-[4-(trifluoromethyl)phenoxy]ethyl(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)carbamate;and
- N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)urea;
  - N-(2-{[4-chloro-3-(trifluoromethyl)phenyl]amino}ethyl)-N'-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)urea;
  - N-{2-[4-chloro-3-(trifluoromethyl)phenoxy]ethyl}-N'-(7-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)urea;
- N-(2-{[4-chloro-3-(trifluoromethyl)phenyl]amino}ethyl)-N'-(6-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)urea; and
  - N-{2-[4-chloro-3-(trifluoromethyl)phenoxy]ethyl}-N'-(6-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)urea
- A medicament comprising the bicyclic amide, carbamate or urea derivative of the formula
   (I), its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof as claimed in claim 1 as an active ingredient.
  - 10. The medicament as claimed in claim 9, further comprising one or more pharmaceutically acceptable excipients.
- 11. The medicament as claimed in claim 9, wherein said bicyclic amide, carbamate or urea derivative of the formula (I), its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof is a VR1 antagonist.
  - 12. The medicament as claimed in claim 9 for the treatment and/or prevention of an urological disorder or disease.

- 13. The medicament as claimed in claim 12, wherein said urological disorder or disease is urge urinary incontinence or overactive bladder.
- 14. The medicament as claimed in claim 9 for the treatment and/or prevention of pain.

- 15. The medicament as claimed in claim 14, wherein said pain is chronic pain, neuropathic pain, postoperative pain, or rheumatoid arthritic pain.
  - 16. The medicament as claimed in claim 9 for the treatment and/or prevention of a disorder or disease related to pain.
  - 17. The medicament as claimed in claim 16, wherein said disorder or disease related to pain is neuralgia, neuropathies, algesia, nerve injury, ischaemia, neurodegeneration, or stroke.
- 10 18. The medicament as claimed in claim 9 for the treatment and/or prevention of an inflammatory disorder or disease.
  - 19. The medicament as claimed in claim 18, wherein said inflammatory disorder or disease is asthma or COPD.
- Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prevention of an urological disorder or disease.
  - 21. Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prevention of pain.
  - 22. Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prevention of an inflammatory disorder or disease.
- 20 23. Process for controlling an urological disorder or disease in humans and animals by administration of a VR1-antagonistically effective amount of at least one compound according to claim 1.
  - 24. Process for controlling pain in humans and animals by administration of a VR1-antagonistically effective amount of at least one compound according to claim 1.
- 25 25. Process for controlling an inflammatory disorder or disease in humans and animals by administration of a VR1-antagonistically effective amount of at least one compound according to claim 1.